

09723722 112800

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GCGGCCTGGGGGGCGCCCCCTGGGGCTGCGGCTGCCCCGGGAGAC
CGACGAAGAGCCCGAGGAGCCCGGCCGGAGGGGCAGCTTTGTGGAGA
TGGTGGACAACCTGAGGGGCAAGTCGGGGCAGGGCTACTACGTGGAG
ATGACCGTGGGCAGCCCCCGCAGACGCTCAACATCCTGGTGGATACA
GGCAGCAGTAACTTTGCAGTGGGTGCTGCCCCCACCCTTCCTGCAT
CGCTACTACCAGAGGCAGCTGTCCAGCACATAACGGGACCTCCGGAAG
GGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGGAGCTGGG
CACCGACCTGGTAAGCATCCCCCATGGCCCCAACGTCACGTGTGCGTGC
CAACATTGCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCC
AACTGGGAAGGCATCCTGGGGCTGGCCTATGCTGAGATTGCCAGGCCT
GACGACTCCCTGGAGCCTTTCTTTGACTCTCTGGTAAAGCAGACCCACG
TTCCCAACCTCTTCTCCCTGCAGCTTTGTGGTGGCTTCCCCCTCAA
CCAGTCTGAAGTGCTGGCCTCTGTGCGGAGGGAGCATGATCATTGGAGG
TATCGACCACTCGCTGTACACAGGCAGTCTCTGGTATACACCCATCCGG
CGGGAGTGGTATTATGAGGTGATCATTGTGCGGGTGGAGATCAATGGA
CAGGATCTGAAAATGGACTGCAAGGAGTACAACCTATGACAAGAGCATTG
TGGACAGTGGCACCACCAACCTTCGTTTGCCCAAGAAAGTGTTTGAAGC
TGCAGTCAAATCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGAT
GGTTTCTGGCTAGGAGAGCAGCTGGTGTGCTGGCAAGCAGGCACCACC
CCTTGGAACATTTTCCAGTCATCTCACTCTACCTAATGGGTGAGGTTAC
CAACCAGTCCTTCCGCATCACCATCCTTCCGCAGCAATACCTGCGGCCA
GTGGAAGATGTGGCCACGTCCCAAGACGACTGTTACAAGTTTGCCATCT
CACAGTCATCCACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTT
CTACGTTGTCTTTGATCGGGCCCCGAAAACGAATTGGCTTTGCTGTCAGC
GCTTGCCATGTGCACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCT
TTTGTACCTTGGACATGGAAGACTGTGGCTACAACATTCCACAGACAG
ATGAGTCAACCCTCATGACCATAGCCTATGTCATGGCTGCCATCTGCGC
CCTCTTCATGCTGCCACTCTGCCTCATGGTGTGTCAGTGGCGCTGCCTC
CGCTGCCTGCGCCAGCAGCATGATGACTTTGCTGATGACATCTCCCTGC
TGAAG

FIG. 1A

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CCATGCCGGCCCCCTCACAGCCCCGCCGGGAGCCCCGAGCCCCGCTGCCCCAGGCTGGC
CGCCGCSGTGCCGATGTAGCGGGCTCCGGATCCCAGCCTCTCCCCTGCTCCCGTGC
TCTGCGGATCTCCCCTGACCGCTCTCCACAGCCCCGACCCGGGGGCTGGCCCAGG
GCCCTGCAGGCCCTGGCGTCCTGATGCCCCCAAGCTCCCTCTCCTGAGAAGCCACC
AGCACCAACCAGACTTGGGGGCAGGCGCCAGGGACGGACGTGGGGCCAGTGCGAGC
CCAGAGGGGCCCGAAGGCCGGGGGCCACCATGGCCCAAGCCCTGCCCTGGCTCCTG
CTGTGGATGGGCGCGGGAGTGCTGCCTGCCCCACGGCACCCAGCACGGCATCCGGC
TGCCCCCTGCGCAGCGGCTGGGGGGCGCCCCCCTGGGGGCTGCGGGCTGCCCCGGG
AGACCGACGAAGAGCCCCGAGGAGCCCCGGCCGGAGGGGCAGCTTTGTGGAGATGGT
GGACAACCTGAGGGGGCAAGTCGGGGCAGGGGCTACTACGTGGAGATGACCGTGGGC
AGCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACCTTTGCAGT
GGGTGCTGCCCCCCCACCCCTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCA
CATACCGGGACCTCCGGAAGGGTGTGTATGTGCCCTACACCCAGGGGCAAGTGGGAA
GGGGAGCTGGGACCGACCTGGTAAGCATCCCCCATGGCCCCAACGTCACTGTGCG
TGCCAACATTGCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCCAACCTGG
GAAGGCATCCTGGGGCTGGCCTATGCTGAGATTGCCAGGCCTGACGACTCCCTGGA
GCCTTTCTTTGACTCTCTGGTAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAG
CTTTGTGGTGCTGGCTTCCCCCTCAACCAAGTCTGAAGTGCTGGCCTCTGTGCGGAGG
GAGCATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGCAGTCTCTGGTATAC
ACCCATCCGGCGGGAGTGGTATTATGAGGTGATCATTGTGCGGGTGGAGATCAATG
GACAGGATCTGAAAATGGACTGCAAGGAGTACAACCTATGACAAGAGCATTGTGGACA
GTGGCACCACCAACCTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGCAGTCAAATCCA
TCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTCTGGCTAGGAGAGCAG
CTGGTGTGCTGGCAAGCAGGCACCACCCCTTGGAACATTTTCCAGTCATCTCACTC
TACCTAATGGGTGAGGTTACCAACCAAGTCCTTCCGCATCACCATCCTTCCGCAGCAA
TACCTGCGGCCAGTGGAAGATGTGGCCACGTCCCAAGACGACTGTTACAAGTTTGCC
ATCTCACAGTCATCCACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTAC
GTTGTCTTTGATCGGGCCCCGAAAACGAATTGGCTTTGCTGTGAGCGCTTGCCATGTG
CACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCTTTTGTACCTTGGACATGGA
AGACTGTGGCTACAACATTCCACAGACAGATGAGTCAACCCTCATGACCATAGCCTA
TGTCATGGCTGCCATCTGCGCCCTCTTCATGCTGCCACTCTGCCTCATGGTGTGTCA
GTGGCGCTGCCTCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTGATGACATCT
CCCTGCTGAAGTGAGGAGGCCCCATGGGCAGAAGATAGAGATTCCCCTGGACCACAC
CTCCGTGGTTCACCTTTGGTCACAAGTAGGAGACACAGATGGCACCTGTGGCCAGAG
CACCTCAGGACCCTCCCCACCCACCAAATGCCTCTGCCTTGATGGAGAAGGAAAAG
GCTGGCAAGGTGGGTTCCAGGGACTGTACCTGTAGGAAACAGAAAAGAGAAGAAAG
AAGCACTCTGCTGGCGGGAATACTCTTGGTCACCTCAAATTTAAGTCGGGAAATTCT
GCTGCTTGAACTTCAGCCCTGAACCTTTGTCCACCATTCTTTAAATTCTCCAACCC
AAAGTATTCTTCTTTTCTTAGTTTTAGAAAGTACTGGCATCACACGCAGGTTACCTTGG
CGTGTGTCCCTGTGGTACCCTGGCAGAGAAGAGACCAAGCTTGTTTCCCTGCTGGC
CAAAGTCAGTAGGAGAGGATGCACAGTTTGCTATTTGCTTTAGAGACAGGGACTGTA
TAAACAAGCCTAACATTGGTGCAAAGATTGCCTCTTGAATT

FIG. 1B

MAQALPWLLLWMGAGVLP AHGTQH GIRLPLR SGLGGAPLGLRLP
RETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPPQT
LNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVPY
TQGWEGELGTDLVSIHPGNVTVRANIAAITESDKFFINGSNWE
GILGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQLCGAGFPLN
QSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRVEIN
GQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEEAAVKSIIKAASST
EKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRIT
ILPQQYL RPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVV
FDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQ
TDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRQQHDDF
ADDISLLK

FIG. 2A

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ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPPQT
LNILVDTGSSNFAVGAAPHPFLHRYRQLSSTYRDLRKGVPY
TQGWEGELGTDLVSIHPNVTVRANIAAITESDKFFINGSNWE
GILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQLCGAGFPLN
QSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRVEIN
GQDLKMDCKEYNYDKSIVDSGTTNLRPKKVFEAAVKSIIKAASST
EKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRIT
ILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVW
FDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQ
TDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRQQHDDF
ADDISLLK

FIG. 2B

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FIG. 3B

ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMT
VGSPQTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKG VYVPYT
QGKWE GELGTDLV SIPHGPNVTVRANI
AAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFFDSL VKQTHVPNLFSLQL
CGAGFPLNQSEVLASVGGGSMIIGGI
DHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNL
RLPKKVFEAAVKSIIKAASSTEKFPD
GFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRTILPQQYL RPVEDVA
TSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGYNIPQTDED
YKDDDDK

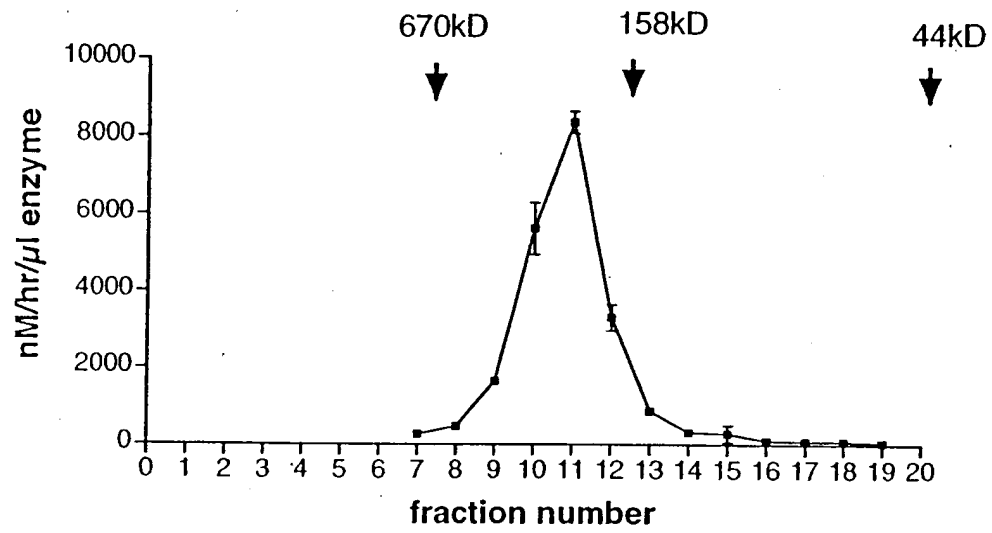
GEC of recombinant β -secretase

FIG. 4



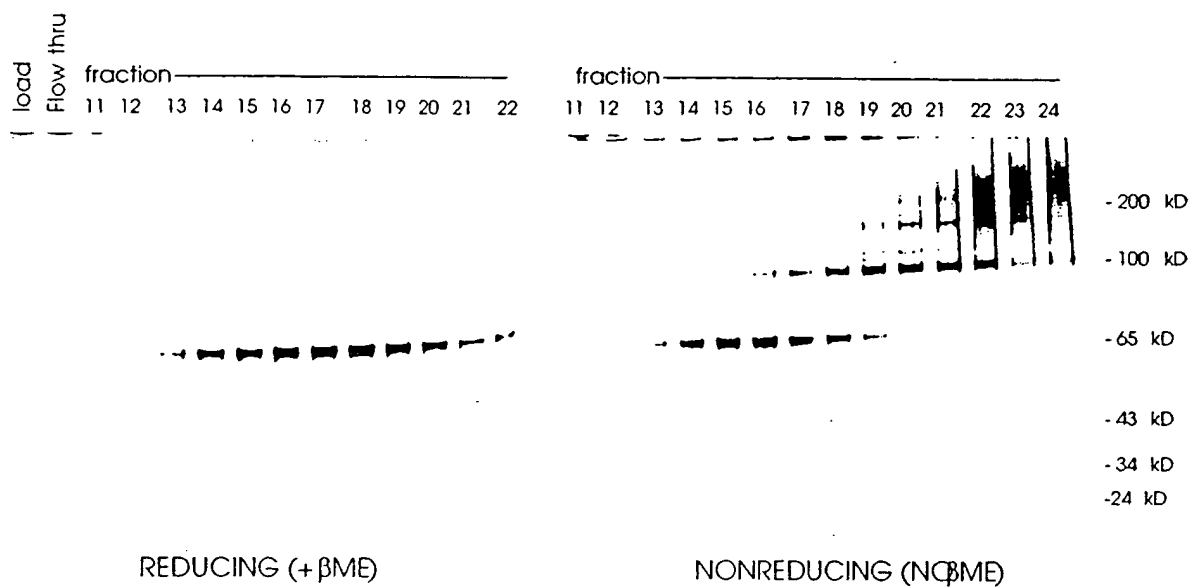


FIG. 6A

FIG. 6B

9/26

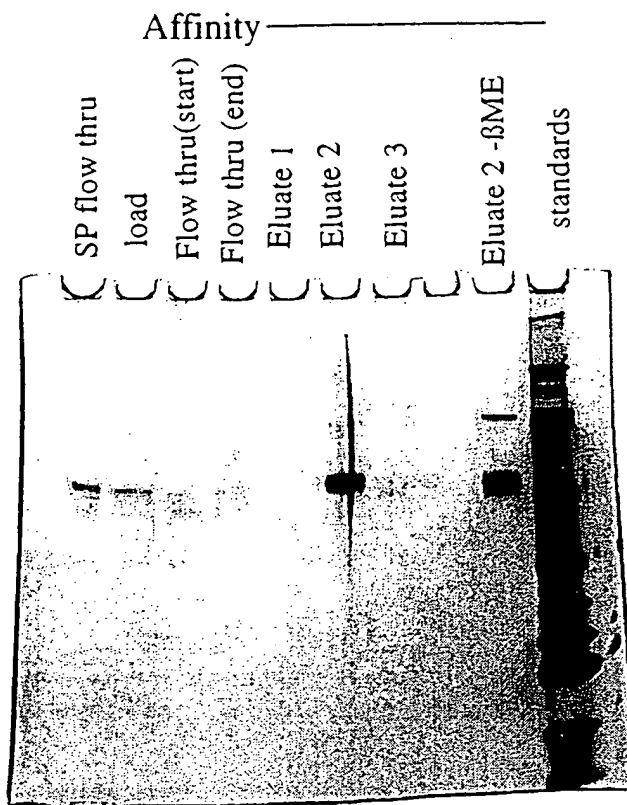


FIG. 7

SP flow thru
SP load
load
Flow thru
Eluate 1
Eluate 2
Eluate 3
293T standard



FIG. 8

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10/26

E T D E E P E E P G R R G S F V E H V D N
 GARACNGAYGARGARCCNGARGARCCNGGNHGNHGNHGNWSNTTYGTNGARATGGTNGAYAAY 63

3427-3430
 5' primer set 1

3431-3434
 3' primer set 1

3448-3451
 5' primer set 2

3452-3455
 3' primer set 2

1^o HNC/primer set 1

(3428+3433)
 54 bp product

1^oHNC & IMR32/ primer set 2

72 bp product

sequence:

set2 3460
 5' RACE primer
 CCCGAAGAGCCCGGCCGAGGGGCAGCTTTGTCTGA 35
 P E E P G R R G S F V
 ORF
 3'RACE primer 3459
 set 2

FIG. 9

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11/26

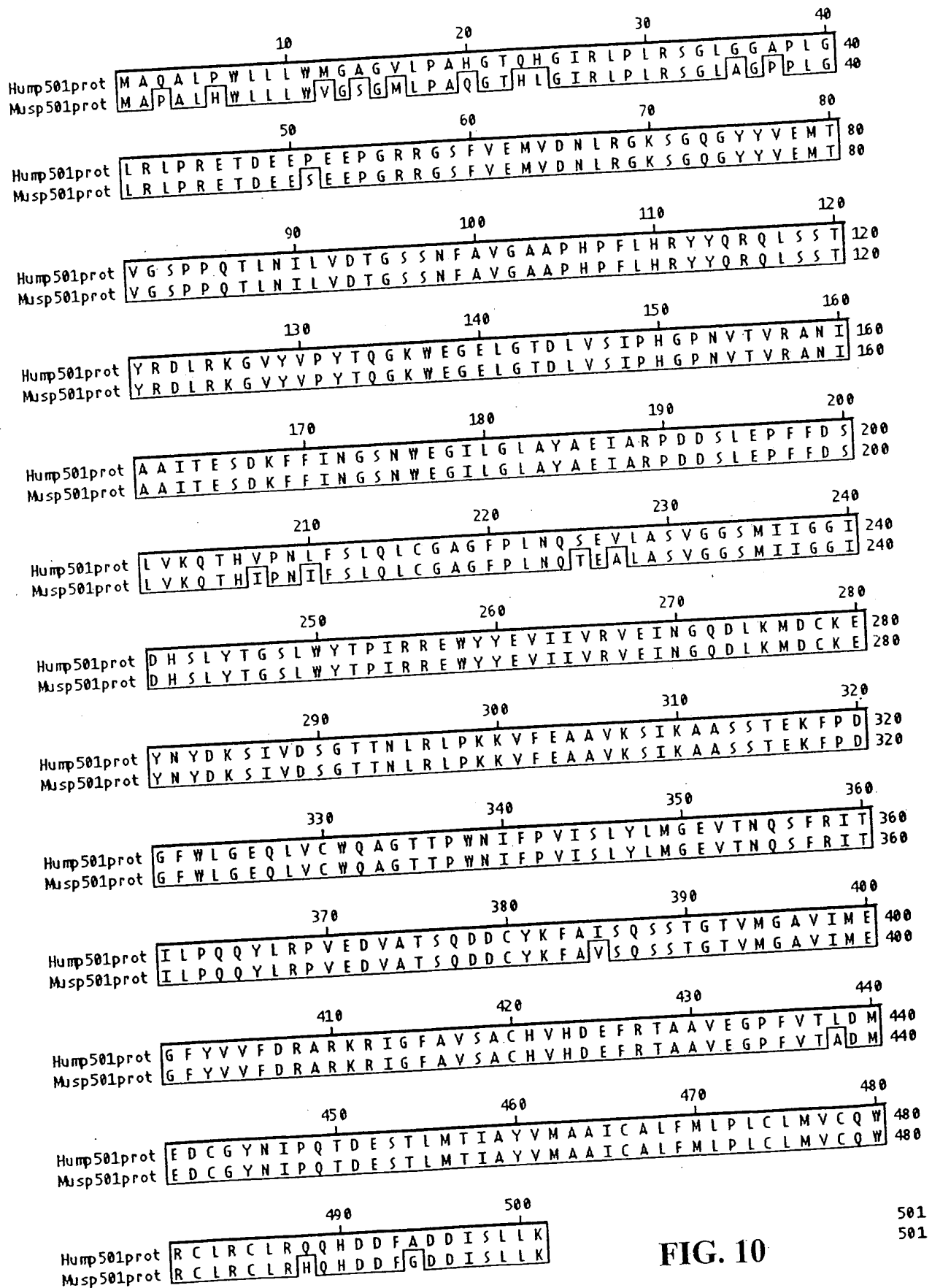
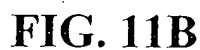


FIG. 10

501
501

FIG. 11A



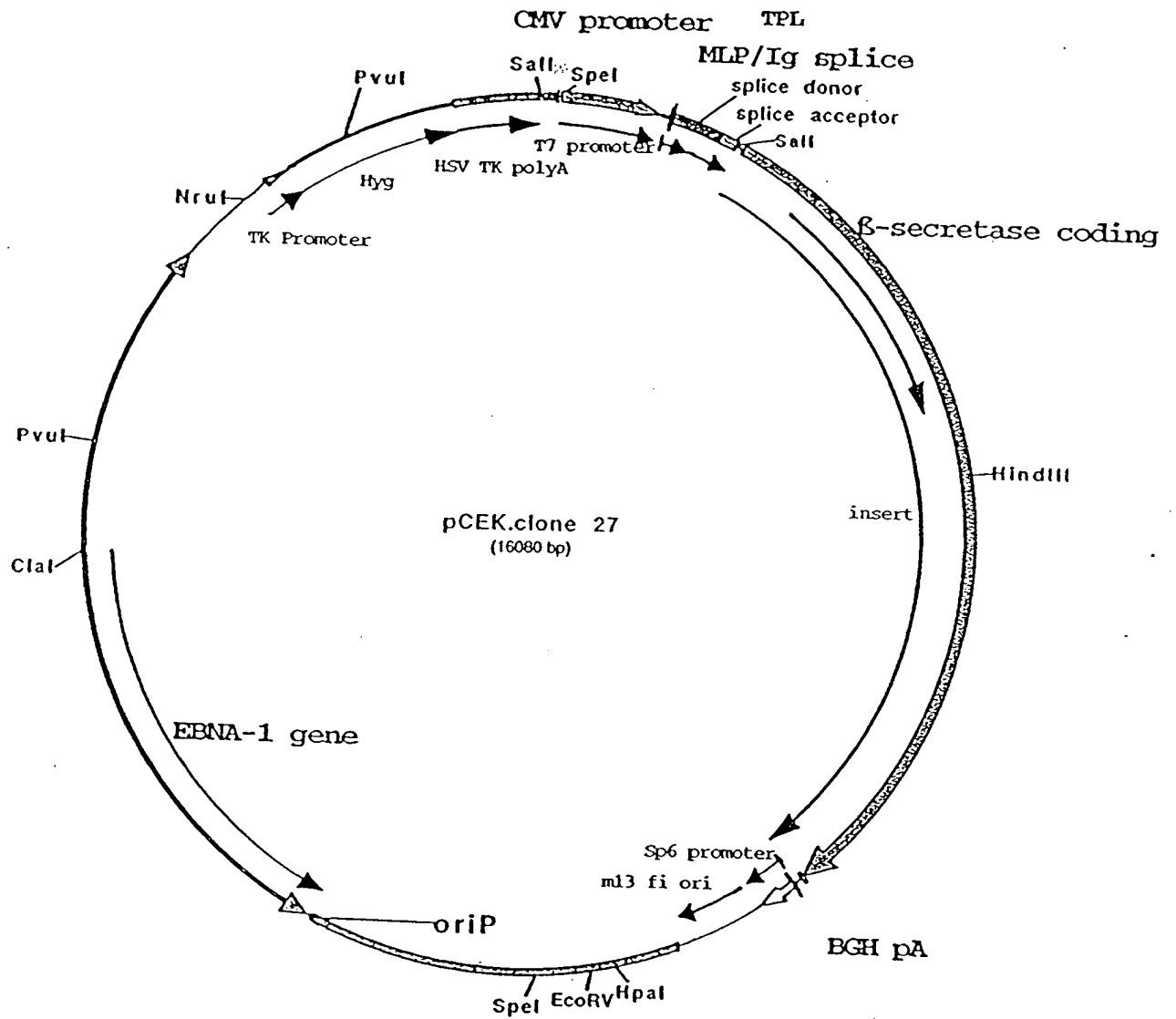


FIG. 12

FIG. 13A

1 TTCTCATGTTTGACAGCTTATCATGCGAGATCCGGGCAACGTTGTTGCATTGCTCCAGGGCAGAACTGGTAAGTATGGAAGATCGATGTACGGGCCAGATATAC
 107 CCGTTGACATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGTCATTAGTTCATAGCCATATATGAGTTCCGGTTACATAAAGTTACGGTAAATGCC
 213 CCGCTGCTGACCGCCCAACGACCCCGCCCATTTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGACTTTCCATTGAAGTCAATGGGTGGACT
 319 ATTTACGGTAAACTGCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTAAGCCCGCTATTGACGTCAATGACGGTAAATGGCCCGCTGCCATTATGCCCA
 425 GTACATGACCTTATGGGACTTTCTACTTGGCAGTACATCTAGTATTAGTTCATGCTATTACATGGTGATCGGTTTTCGAGTACATCAATGGCCGTGGATAG
 531 CGGTTTGACTCACGGGGATTTCGAAGTCTCAACCCATTGACGTCAATGGGAGTTTGTTTTCGCAACAAAATCAAGGGGACTTTCCAAAATGTGTAACAACATCCG
 637 CCCCATTGACGCAAAATGGCGGTAGGGGTGTACGGTGGAGGCTATATAAGCAGAGCTCTCTGGCTAACTAGAGAACCCATGCTTACTGGCTTATCGAAATTAA
 743 TACGACTCACTATAGGAGACCCAACTCTGTTGGGCTCGGGTTGAGGACAACTCTTCCGGCTCTTCCAGTACTCTTGGATGGGAAACCGCTCGGCTCCGAA
 849 CGGTACTCCGCCACCGAGGGACCTGACCGAGTCCGCATCGACCGATCGGAAACCTCTCGACTGTTGGGTGAGTACTCCCTCTCAAAAGGGGATGACTTCTG
 955 CCTAAGATTGTTCAGTTTCCAAAACGAGGAGGATTGTATTCACCTGGCCCGCGTGATGCCCTTGAGGGTGGCGCGTCCATCTGGTCAGAAAAGCAATCTT
 1061 TTTGTGTCAAGCTTGAGGTGTCCAGGCTTGAGATCTGCCCATACACTTGAGTGACAAATGACATCCACTTTGCCCTTCTCTCCACAGGTGCCACTCCAGGTCC
 1167 AACTGCAGGTGACTCTAGACCCGGGAATTCTGCAGATATCCATCACACTGCGCGACTCGTCCCGACCCCGCCCGGAGCTCCGAGCCCGAGCTGGATTATGG
 1273 TGGCTGAGCAACGACGAGCCGAGGACCCGAGCCCTTGCCCTTCCCTCCCGCCCGCGCGCGCGGGGAGCCAGGGAAGCCGCCACCGCCCGCCATGCCCG
 1379 CCGCTCCAGCCCGCCGGGAGCCCGCCCGCTGCCAGGCTGGCCCGCCCGCTGCCGATGTAGCGGCTCCGGATCCAGCCCTTCCCTGCTCCCGTCTCTG
 1485 CGGATCTCCCTGACCGCTCTCCACAGCCCGGACCCCGGGCTGGCCAGGGCCCTGCAGGCCCTGGGTCTGTATGCCCAAGCTCCCTCTCTGAGAAGCCAC
 1591 CAGCACCCAGACTTGGGGCAGCGCCAGGACCGACGTGGGCCAGTGGAGCCAGAGGGCCCGAAGGCCCGGGCCACC ATG GCC CAA GCC CTG
 1690 CCC TGG CTC CTG CTG TGG ATG GGC GCG GGA GTG CTG CCT GCC CAC GGC ACC CAG CAC GGC ATC CCG CTG CCC CTG GCG
 6 Pro Trp Leu Leu Trp Met Gly Ala Gly Val Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg
 1768 ACC GGC CTG GCG GGC GCC CCC CTG GCG CTG CCG CTG CCC CCG GAG ACC GAC GAA GAG CCC GAG GAG CCC GGC CCG AGG
 32 Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg
 1846 GGC AGC TTT GTG GAG ATG GTG GAC AAC CTG AGG GGC AAG TGG GCG CAG GGC TAC TAC GTG GAG ATG ACC GTG GGC AGC
 58 Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser
 1924 CCC CCG CAG ACG CTC AAC ATC CTG GTG GAT ACA GGC AGC AGT AAC TTT GCA GTG GGT GCT GCC CCC CAC CCC TTC CTG
 84 Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu
 2002 CAT GGC TAC TAC CAG AGG CAG CTG TCC AGC ACA TAC CCG GAC CTC GCG AAG GGT GTG TAT GTG CCC TAC ACC CAG GGC
 110 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly
 2080 AAG TGG GAA GCG GAG CTG GGC ACC GAC CTG GTA AGC ATC CCC CAT GGC CCC AAC GTC ACT GTG GGT GGC AAC ATT GCT
 136 Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala
 2158 GGC ATC ACT GAA TCA GAC AAG TTC TTC ATC AAC GGC TCC AAC TGG GAA GGC ATC CTG GCG CTG GCC TAT GCT GAG ATT
 162 Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile
 2236 GGC AGG CCT GAC GAC TCC CTG GAG CCT TTC TTT GAC TCT CTG GTA AAG CAG ACC CAC GTT CCC AAC CTC TTC TCC CTG
 188 Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu
 2314 CAG CTT TGT GGT GCT GGC TTC CCC CTC AAC CAG TCT GAA GTG CTG GGC TCT GTC GGA GCG AGC ATG ATC ATT GGA GGT
 214 Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly
 2392 ATC GAC CAC TCG CTG TAC ACA GGC AGT CTC TGG TAT ACA CCC ATC CCG CCG GAG TGG TAT TAT GAG GTC ATC ATT GTG
 240 Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val
 2470 CCG GTG GAG ATC AAT GGA CAG GAT CTG AAA ATG GAC TGC AAG GAG TAC AAC TAT GAC AAG AGC ATT GTG GAC AGT GGC
 266 Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly
 2548 ACC ACC AAC CTT CGT TTG CCC AAG AAA GTG TTT GAA GCT GCA GTC AAA TCC ATC AAG GCA GCC TCC TCC ACG GAG AAG
 292 Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys
 2626 TTC CCT GAT GGT TTC TGG CTA GGA GAG CAG CTG GTG TGC TGG CAA GCA GGC ACC ACC CCT TGG AAC ATT TTC CCA GTC
 318 Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val

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2704 ATC TCA CTC TAC CTA ATG GGT GAG GTT ACC AAC CAG TCC TTC GGC ATC ACC ATC CTT CGG CAG CAA TAC CTG GGC CCA
344 Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro

2782 GTG GAA CAT GTG GGC AGC TCC CAA GAC GAC TGT TAC AAG TTT GGC ATC TCA CAG TCA TCC AGC GGC ACT GTT ATG GCA
370 Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly

2860 GGT GTT ATC ATG CAG GGC TTC TAC GTT GTC TTT GAT GGG GGC CCA AAA CCA ATT GGC TTT GCT GTC ACC GCT TCC CAT
396 Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His

2938 GTG CAC GAT GAG TTC AGC AGC CCA GCG GTG GAA GGC OCT TTT GTC ACC TTG CAC ATG GAA GAC TGT GGC TAC AAC ATT
422 Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile

3016 CCA CAG ACA GAT GAG TCA ACC CTC ATG ACC ATA GGC TAT GTC ATG GCT GGC ATC TCC GGC CTC TTC ATG CTG CCA CTC
448 Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ile Cys Ala Leu Phe Met Leu Pro Leu

3094 TCC CTC ATG GTG TGT CAG TGG GGC TCC CTC GGC TCC CTG GGC CAG CAG CAT GAT GAC TTT GCT GAT GAC ATC TCC CTG
474 Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser Leu

3172 CTG AAG TGA GGAGGCCATGCGCAGAGATAGAGATTGCGCTGCAACACCTCGGTGCTTCCTTTGTCACAAGTAGGAGACACAGATGCGACCTGTGCGC
500 Leu Lys ...

3275 AGACCACTCAGGACCTGCGCAACCAACAAATGCTCTGCTTTGATGAGAAGGAAAGGCTGCAAGGTGGGTTCAGGACTGTACCTGTAGGAACAGAAAA
3381 GAGAAGAAGAAGCACCTCTGCTGCGGAATACCTCTGCTCACTCAATTTAAGTGGGAAATTCCTGCTCTGAACTTCAGGCTGAACCTTTGTCCACCAT

3487 CCTTTAAATTCCTCAACCCAAAGATTCTCTTTCTTTCTAGTTTCAGAAGTACTGTCATCACAGCAGGTACCTTTGGGTGTGCTGCTGTGTAACCTGCGCAGAGA

HindIII

3593 AGAGACCAAGCTTGTTTGCGCTGCGCAAGTCACTAGAGAGGATGCACAGTTTCTATTGCTTTAGAGACAGGACTGTATAAACAAGCTTAACATTGGTGC

3699 AAAGATTGCTCTTGAATTAAAAAAGAACTAGATTGACTATTATACAAATGCGCGCGCTGGAAGAGAGAGAGGAGAGGAGTACAAAGACAGGAAATAGTG

3805 GGATCAAGCTAGGAAAGCGAGAAACACAACCACTCACCAGTCTAGTTTATAGACTCATCTCCAGATAGCATCCCATCTCAGAAGATGGGTGTTGTTTCAATG

3911 TTTTCTTTTCTGTGTTGCGGCTGACGAAAGTGCAGATGGGAGGGCTTATCTAGCCAAAGAGCTCTTTTATAGCTCTCTTAAATGAAGTGGCCACTAAGAAGTT

4017 CCACCTTAACACATGAATTTCTGCCATATTATTTCAATTGCTCTATCTGAACCAACCTTTATCTACATATGATAGGACGACTGAAATATCTAAACCCCTAAGC

4123 TCCAGGTGCGCTGCGGAGAGCACTGACTATAGCAGGGCTGGGCTCTGCTCTCTGCTGTCATAGGCTCACTCTTTCCCCCAATCTTCTCTGAGGCTTTGCGC

4229 CAAGGTGCTAAAGGAATAGTATGAGAGACTCTCTATCTAATCTTAAAGCATAATGTTGAACATTCATTCAACAGCTGATGCTTATAACCCCTGCTGGATT

4335 TCTTCTATTAGCTATAGAAAGTAGCAGATCTTTACATAATTCAGAGTGGTTTCATGCGCTTCTAAGCTCTAATGGGCTTCAATTATTTGACTAAGCA

4441 TCACACAGTGGCACTAGCATTATACCAAGAGTATGAGAAATACAGTCTTTATGCTCTAACATTAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCTTCAAGCT

4547 CCTGAGGCTTCTTATGCTGCTCAACCAAGAGCTCTGATGAAGTCACTCTTTTCCCTATCTGTTCTTCCCTGCGGCTCTCTAATGGTAACTGAGTGGTAC

4653 CAGGCTGTTCTTGGCTAGGTAGTGGGACCAAGTTCACTAAGCTCTATCAGTTCTAGCATAGTAACTAAGTAACTGTTAGTGGGAGAGCTGGGTTTTC

4759 CTAGTATACCACTGATCTACTCTAAGCTGTCAGGCTGCTTCCAGGTATGGGAGCTCTAAGTGTGAATTACCTGATAAGGAGAGGAAATACAGCA

4865 GGGCTCTGGTGTCTGCTGCGCTCAGGCACTGCGCAGGCAATACCAATAAACAAGAATACCTGAGTCAAGTTTATCTGGTCTCTTCACTTCCACTGCA

4971 CTTGCTGCTCTTTGCTGACTGGAACACCCATAACTACAGAGTCTGACAGGAGCTGAGACTGTGCACTTCTAGCTGGAAGTACTGTGTAAATAAAGTT

5077 TCAGAAGCTTACCATGAAGTGAATGCAATTTTCTTTATAATTTCTAAGCATGTTGGGAAAGTGGCTTTTCCAGGCTTTCCAGGCAATAAAGTTCA

5183 ACCCTTGCATAGCAAGTCCCATCAGCTATTATTTTAAAGAAAGTTGCACTTGTCTTTTCTTTTACAGTTACTTCTTCTGCGGCAAAATATAAAGTTCT

[illegible][illegible]

FIG. 13D

[illegible]

FIG. 13E

15041 CTGCCAAACTGTGATGACGACACCGTCAGTGGGTCCGTCCGCCAGGCTCTCGATGAGCTGATGCTTTTGGGCGAGGACTGCCCGGAGTCCGGCACTCGTGCAC
15147 GCGATTTCCGCTCCAACAATGTCTTGACCGACAAATGCCCCATAACAAGGTCATTGACTGCGAGCGAGGCGATGTTCCGGGATTCCTCAATACGAGGTGCCAACA
15253 TCTTCTTCTGGAGGCGGTGGTTGCCCGGTATGAGCGAGCAGACCGCTACTTGCAGGCGAGGCACTCCGAGCTTCCAGGATCCCGCGGCTCCCGGCGTATATGCT
15359 CCGCATTTGCTTTGACCAACTCTATCAGAAGTTGGTTGACCGCAATTTGATGATGCAAGCTTGGCGCAAGGTGGATCCGACCAATGTTCCGATCCGAGCGCGG
15465 ACTGTCCCGGTACACAAATGCCCGCAGAGCGGCGGTCTGACCGATGGCTGTGTAGAAGTACTGCCGATAGTGGAAACCGGAGATGGGGAGGCTAACTG
15571 AAACAAGGAGAGACAATACCGAAGGAAACCGCGCTATGAAGCAATAAAAGACAGAATAAAAGCAAGGCTGTTGGTGGTTTGTTCATAAACCGCGGTTTC
15677 GGTCCAGGCTGGCACTCTGTGATACCCACGAGACCCCATTTGGGCGCAATAGGCGCGGTTTCTTCTTTTCCACCCCAACCCCAAGTTGGGTGAAGG
15783 CCGAGGCTGGCAGCCAAGTGGGGGGGCGGCGCTGCATAGGCACTGGGCGGTTGGTTAGGAGCGGGTCCCGCATGGGGAATGGTTATGGTTGGTGGGG
15889 TTATTATTTTGGGCTGGGTGGGCTGGTGCAGGCTGGCTGAGCAGACAGAACCATGTTTTCGATGGCTGGCATGGAACCATGTACTGGCGGACAC
15995 GAACACCGGCGGTCTGTGGCTGCCAAACACCCCGAAGCCCAAAAACCAAGGCGGATTTCTGGGTGCCAAGCTAGTGAACAA

Sall

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CTGTTGGGCTCGCGGTTGAGGACAAACTCTTCGCGGTCTTTCCAGTACTCTTGGATCGGAAAC
 CCGTCGGCCTCCGAACGGTACTCCGCCACCGAGGGACCTGAGCGAGTCCGCATCGACCGGAT
 CGGAAAACCTCTCGACTGTTGGGGTGAGTACTCCCTCTCAAAGCGGGCATGACTTCTGCGCT
 AAGATTGTCAGTTTCCAAAAACGAGGAGGATTTGATATTACCTGGCCCGCGGTGATGCCTTT
 GAGGGTGGCCGCGTCCATCTGGTCAGAAAAGACAATCTTTTTGTTGTCAAGCTTGAGGTGTGG
 CAGGCTTGAGATCTGGCCATACACTTGAGTGACAATGACATCCACTTTGCCTTTCTCTCCACAG
 GTGTCCACTCCCAGGTCCAACCTGCAGGTGCACTCTAGACCC

FIG. 14A

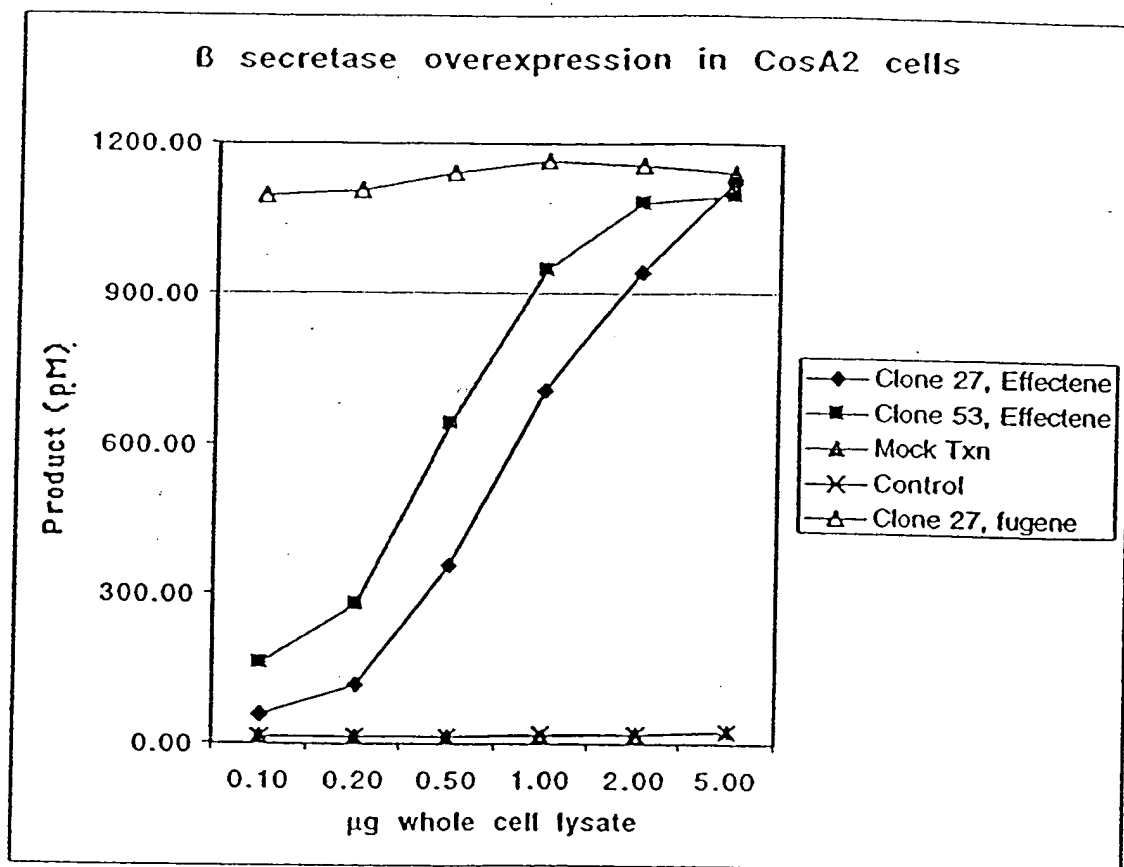


FIG. 14B

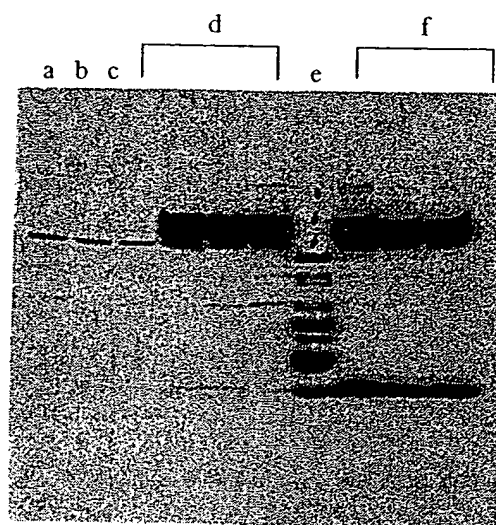


FIG. 15A

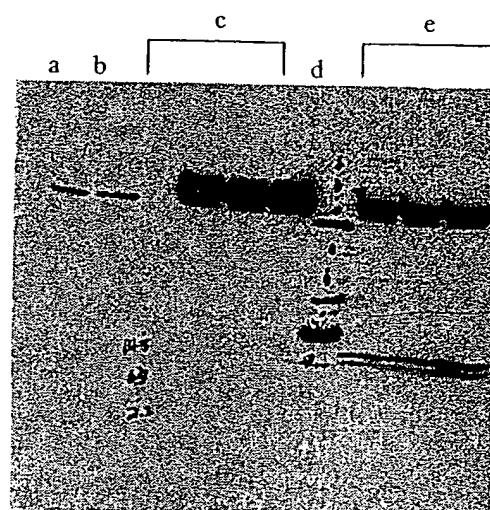
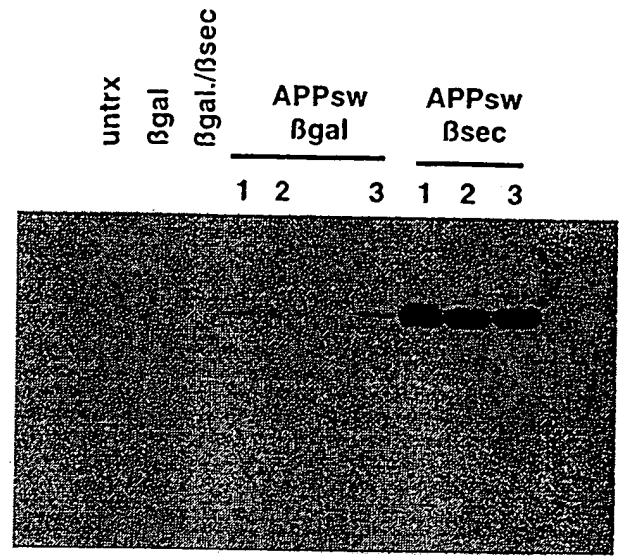
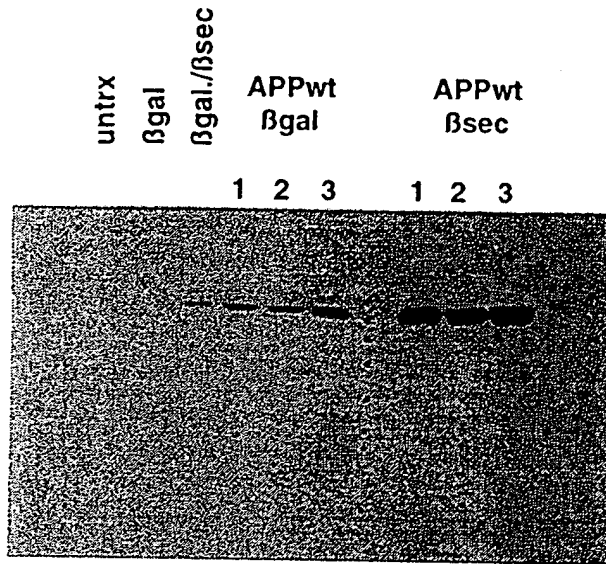


FIG. 15B

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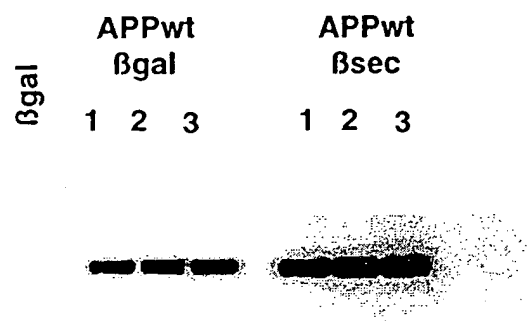


FIG. 17A



FIG. 17B

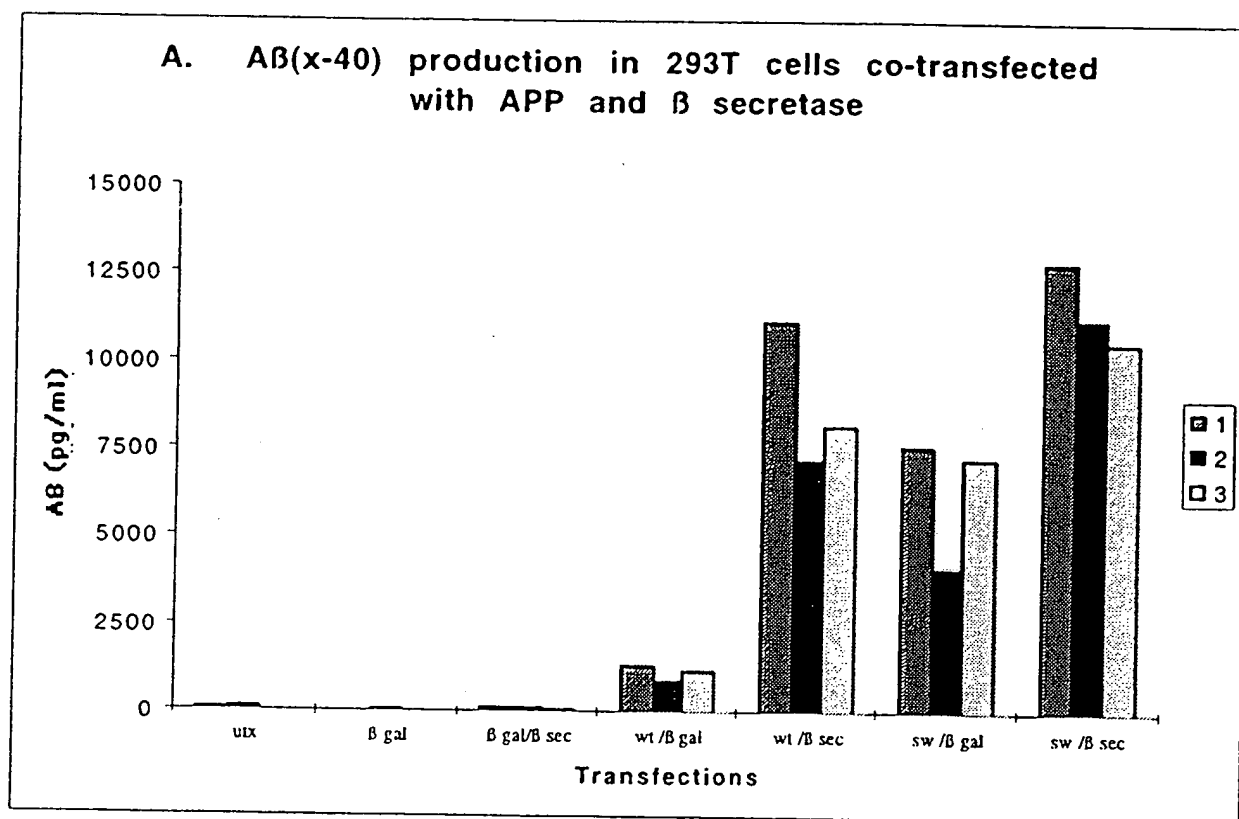


FIG. 18



FIG. 19B



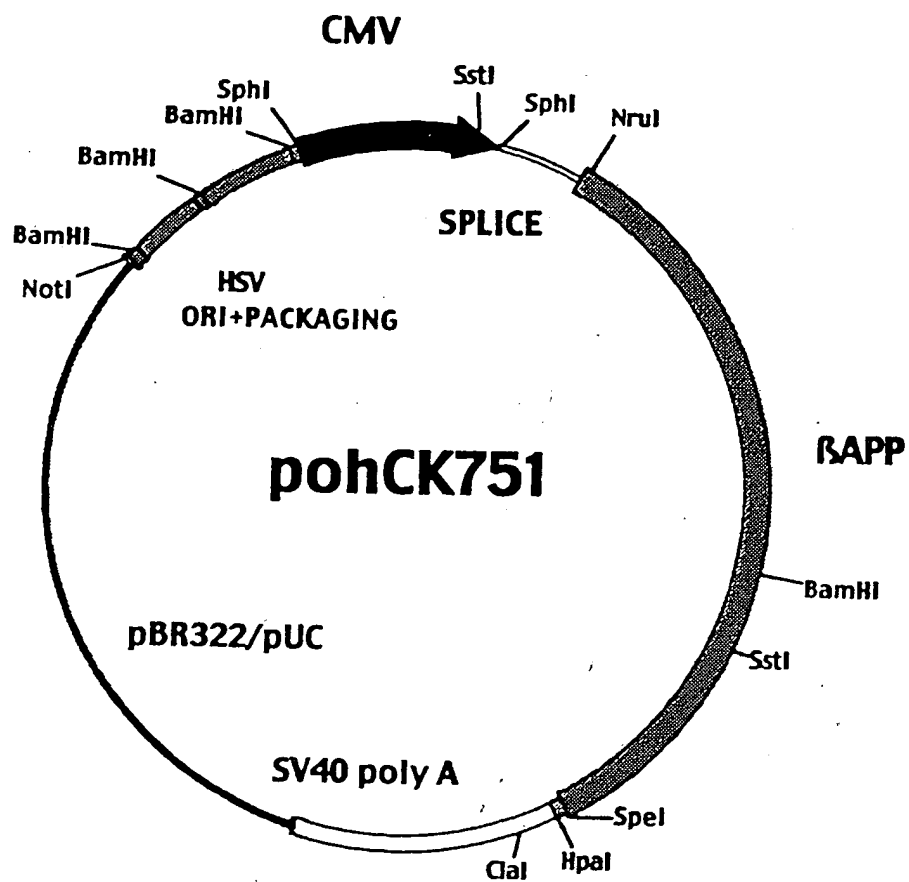


FIG. 21

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